

PATENT SPECIFICATION

(11) 1384 599

1384 599

- (21) Application No. 20781/72 (22) Filed 4 May 1972
 (23) Complete Specification filed 5 July 1973
 (44) Complete Specification published 19 Feb. 1975
 (51) INT CL² C11D 17/00 (C11D 17/00 9/44 9/50)
 (52) Index at acceptance
 C5D 6B12B1 6B12E 6B4 6B5 6C9
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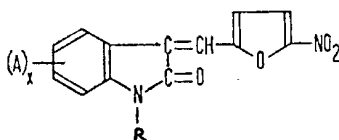


(54) COLOURED DETERGENT COMPOSITIONS

(71) We, COLGATE-PALMOLIVE COMPANY, a Corporation organised under the Laws of the State of Delaware, United States of America, of 300 Park Avenue, New York, New York 10022, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to anti-bacterial detergent compositions, particularly ionic detergent compositions.

According to the present invention a multi-coloured detergent composition comprises a detergent and in discrete regions of the composition which contrast in colour to other regions of the composition, an anti-bacterial amount of an oxindole compound of the formula



wherein A represents C₁—C₃₀ alkyl, C₁—C₃₀ alkoxy, C₂—C₃₀ alkoxyalkyl, hydroxy, halogen, carboxy, C₂—C₃₀ carbalkoxy, nitro, amino, C₁—C₃₀ mono- or di-alkylamino, C₁—C₃₀ acylamino, C₁—C₃₀ alkylsulphonyl or C₂—C₃₀ acyloxy; R represents hydrogen or C₁—C₃₀ acyl; and x represents 0 to 4, as the sole or partial colouring agent for the discrete regions.

The specified oxindole compounds exhibit outstanding anti-bacterial activity and are highly efficacious against a wide variety of Gram negative and Gram positive organisms when employed in conjunction with an ionic detergent, e.g. anionic, cationic, ampholytic or zwitterionic surface-active detergent substances, and particularly with anionic detergent materials such as soap. There is also a high degree of skin substantivity of the oxindole compounds, particularly when applied

from ionic detergent carrier materials, whereby there results a persistent anti-bacterial activity on the skin for extended periods of time after contact therewith.

The invention also makes use of another property of the specified oxindole compounds, namely their colour. In the compositions of the invention these compounds are not present throughout the compositions but are segregated into discrete regions which contrast in colour with other regions of the compositions, providing a multi-coloured or variegated effect. The colours of the specified oxindole compounds range from yellow to red, and the regions containing these compounds have a hue deriving from their colour. The other regions will have a contrasting colour, e.g. white or off-white, such as the natural colour of the ionic detergent and/or other components of the composition. In the case of soap bars, these may have a variegated or marbled appearance. Detergent powders may have a speckled appearance. Liquids, too, may be multi-coloured, e.g. comprising two or more immiscible phases of different colours.

In the above formula for the oxindole compounds, the preferred compound is 3 - (5 - nitrofurfurylidene) oxindole, i.e. x=0 and R=hydrogen. However, where A is an organic group, it is preferably C₁ to C₈ alkyl, C₁ to C₈ alkoxy, C₂ to C₁₆ alkoxyalkyl, C₂ to C₈ carbalkoxy, C₁ to C₈ alkylamino, C₁ to C₁₂ acylamino, C₁ to C₈ alkylsulphonyl, or C₂ to C₈ acyloxy; and where R is an acyl group it is preferably C₂ to C₈ acyl.

Among the suitable anionic detergents are water-soluble soaps and sulphated or sulphonated synthetic detergents. The soaps useful in performing the invention are generally water-soluble salts of fatty acids (including rosin acids) which are derived usually from fats, oils and waxes of animal, vegetable or marine origin, e.g. tallow, coconut oil, tall oil and palm kernel oil. Particularly preferred soaps are the sodium and/or potassium salts of coconut oil-tallow mixtures in weight ratios of 10—60 parts of the coconut oil salts to 90—40 parts of the tallow salts.

With respect to the sulphonated synthetic detergents, it is preferred to employ a higher alkyl aryl sulphonate such as an alkyl benzene sulphonate detergent wherein the alkyl group has from 8 to 18 carbon atoms. Suitable examples are sodium decyl benzene sulphonate, sodium dodecyl and pentadecyl benzene sulphonates wherein the dodecyl and pentadecyl groups are derived from a propylene polymer, and linear alkyl benzene sulphonates such as sodium keryl benzene sulphonate. Other suitable agents are surface-active water-soluble sulphated or sulphonated aliphatic compounds, preferably having 8 to 22 carbon atoms. Examples thereof are alkyl sulphonates and sulphuric acid esters of polyhydric alcohols incompletely esterified with higher fatty acids (e.g. sodium coconut oil monoglyceride monosulphate); long-chain pure or mixed alkyl sulphates (e.g. sodium lauryl sulphate, coconut fatty alcohol sulphate); sulphate of the ethoxylated aliphatic alcohols such as a ammonium lauryl alcohol triethoxamer sulphate; fatty acid ethanolamide sulphate (e.g. sodium coconut fatty acid ethanolamide sulphate); fatty acid amides of amino alkyl sulphonic acids (e.g. sodium lauric acid amide of taurine); and fatty acid esters of isethionic acid. These anionic surface-active agents are used generally in the form of their water-soluble salts, as the alkali metal (e.g. sodium or potassium) salts, though other water-soluble salts such as ammonium, alkylolamine and alkaline earth metal salts may be used if desired.

Other suitable anionic detergents include synthetic detergents having a carboxylate group, and particularly fatty acid amides of aliphatic amino acid compounds. Typical examples are fatty acyl sarcosinates having 10 to 18 carbons, usually 12 to 14 carbons, in the acyl radical, preferably the water-soluble salts of N-lauroyl or N-cocoyl sarcosine. Other materials are fatty acid amides of peptide amino acids obtained by protein obtained by protein hydrolysis known as "Lamepons" and "Maypons" (Lamepon and Maypon are trade marks). Other suitable detergents with carboxylate groups are various cationic and amphoteric detergents described hereinafter. Suitable ether-containing sulphates may be used, such as alkylphenol polyglycol ether sulphates, e.g. lauryl phenol polyethyleneoxy sulphates, and alkyl polyglycol ether sulphates, e.g. lauryl ethyleneoxy sulphates, each containing 10 to 18 carbons in the alkyl groups and usually averaging 2 to 10 moles of ethylene oxide, more usually 3 to 4 moles, per molecule.

Cationic detergents wherein a quaternary nitrogen is part of an open chain or heterocyclic structure may also be used alone or in combination with other compatible detergents. Suitable salts include the chloride, bromide, acetate, sulphate and methosulphate.

Examples are lauroyl pyridinium bromide, N-(lauroyl colamino formylmethyl) pyridinium chloride, cetyl trimethyl ammonium chloride, cetyl pyridinium chloride, stearyl or oleyl dimethylbenzyl ammonium chloride, stearyl amine acetate and stearyl dimethyl amine hydrochloride.

Other suitable surface-active agents which can under certain conditions have a cationic nature and which may be used include alkyl amine oxides such as lauryl dimethyl amine oxide. In place of the lauryl radical, other long chain alkyl radicals, preferably having 10 to 18 carbon atoms, may be used. In place of either or both methyl radicals, there may be other alkyl or hydroxyalkyl radicals such as those having 2 carbon atoms each. Suitable examples include a mixture of higher alkyl dimethyl amine oxides having 12 to 14 carbon atoms in the higher alkyl groups.

Any amphoteric (ampholytic) deterative materials may also be employed. Among these are alkyl imidazolines, such as 1 - coco - 5 - hydroxyethyl - 5 carboxy - methyl imidazoline known as "Miranol CM", and alkyl beta-alanines such as dodecyl beta-alanine known as "Deriphats" (Deriphats is a trade mark), these materials having usually an alkyl group of 10 to 18 carbons and the carboxylate group being in the form of a water-soluble salt. Further examples are the disodium salt of 1 - lauryl - cycloimidium - 2 - ethoxy - ethionic acid - 2 - ethionic acid and its corresponding 2-lauryl sulphate derivative.

The oxindole compound is generally present in the composition in an amount of from 0.01% to 10% by weight of the detergent composition, preferably from 0.5% to 2%. An excellent product is a soap bar comprising milled and plodded soap chips prepared from 20% sodium coconut oil soap and 80% sodium tallow soap and containing 0.5 to 1.5% by weight of 3 - (5 - nitrofur-furylidene) oxindole.

As already indicated, the detergent compositions of this invention may be of various forms, such as soap bars, spray dried and granulated solid compositions, synthetic non-soap detergent bars, combination soap-synthetic detergent bars and liquid detergent compositions. The compositions may have various uses, e.g. as pre-surgical scrubbing compositions which are widely employed in the medical field. The last-mentioned detergent compositions contain a detergent such as a potassium soap, a triethanolamine lauryl sulphate or a sodium lauryl ether sulphate. The detergent compositions of this invention may also be formulated for use as shampoos. Other examples include scouring cleanser compositions as well as other hard surface cleaners, toothpastes, toothpowders, mouth washes and other oral products which include a detergent and

for which effective germicidal activity is desired.

Various other ingredients can be included in addition to the specified oxindole compound and the detergent, such as inorganic water-soluble builder salts. Among the most common of these compounds are the water-soluble salts, usually alkali metal or ammonium salts, of sulphuric, phosphoric, silicic, carbonic, boric and hydrochloric acids, and derivatives thereof. Useful builder salts are polyphosphates, sodium and potassium sulphate, sodium carbonate, sodium silicate, sodium bicarbonate, sodium perborates, borax, sodium chloride and sodium phosphates such as disodium hydrogen phosphate, to name only a few.

Various other adjuvant ingredients may be added as desired, including compatible perfumes, additional colouring materials, corrosion or tarnish inhibitors, fluorescent brighteners, thickeners, solvents, lubricants (to promote flowability), foam enhancers and stabilizers, waxes and colloidal materials such as bentonite. These adjuvants are usually present in minor amounts, rarely exceeding 20% by weight and often totalling about 5%, and are usually incorporated to improve specific aesthetic or performance characteristics. The amount of solvent may be as much as half of a liquid detergent composition. If desired, the specified oxindole compound may be initially dissolved in a suitable solvent before introduction into a detergent system.

In view of the fact that the specified oxindole compounds are highly coloured, as has already been mentioned, it has been found particularly suitable and desirable to make multi-coloured soap bars wherein one colour component (e.g. red) is supplied by the oxindole compound and the other by the colour of the soap itself, which generally ranges from white through off-white to ivory.

In producing multi-coloured soap bars, various techniques may be employed, and particular mention may be made of the marbling process described in United States Patent No. 3,485,905 and to the corresponding apparatus for carrying out such a process as described in United States Patent No. 3,609,828. Other techniques for producing multicoloured, variegated, striped and otherwise marbled and striated soap products are described in British Patent Application No. 58322/71 (Serial No. 1370670).

Various coloured soap and other detergent products can also be produced by blending with the oxindole compound a second or further colour factor, as by the addition of a differently coloured pigment or dyestuff. In this manner a wide spectrum of coloured products may be produced.

It has been found that at the usual concentrations of oxindole compound as described herein, even at the lowest levels, outstanding

multi-coloured products are produced by the techniques generally available in the art, and specifically in those publications cited above.

If it is so desired, one may suitably encapsulate the oxindole compound in a transparent encapsulating material and incorporate the encapsulated product in the detergent.

In evaluating compositions embodying the invention, several different techniques are available and among these mention may be made of the following:

A. Streak Test

This test comprises adding a bacteriostat-containing detergent solution to a predetermined amount of warm tryptone glucose extract agar, in an amount sufficient to obtain the desired concentration of bacteriostat in the agar fluid. This fluid mixture is then poured into a Petri dish and allowed to harden. A 4mm standard loop of an overnight broth culture of *Staphylococcus aureus*, FDA (United States Food and Drug Administration) strain 209, is then added to the Petri dish and uniformly distributed over the surface of the hardened agar. The Petri dish is then incubated for 48 hours at 37° C and the bacterial growth is rated as follows:

0 = no growth
+ = slight growth
+2 = medium growth
+3 = heavy growth

B. Time Kill Test

This test was developed by Cade and Halverson (Cade, A.R., and Halverson, H. O., SOAP, Vol. 10, No. 9, Page 25). This test comprising the steps of preparing an aliquot of a detergent solution from a soap or other detergent composition containing the desired amount of bacteriostatic composition. This solution is then added to FDA nutrient broth in amounts such as to obtain the desired concentration of bacteriostat in the broth. The broth-detergent-bacteriostat fluid is then heated at 37° C in a water bath and inoculated with a 0.1 ml solution of a standard overnight culture of *Staphylococcus aureus* (FDA 209) (or other bacteria being employed). After 10 minutes of incubation, an aliquot of the mixture is removed and diluted in 0.1% peptone water diluent and mixed with a certain amount of warm trypticase soy agar. This final mixture is then poured into a Petri dish and, after solidification of the agar, the Petri dish is incubated at 37° C for 24 hours. In this period of incubation, surviving bacteria cells mature into bacteria colonies. These are then counted in a regular Quebec colony counter. The resulting figure represents the number of bacteria cells which survived a ten minute exposure to the anti-bacterial composition.

C. Serial Dilution test

In order to determine the minimum amount of the anti-bacterial agent needed to inhibit the bacteria growth the Serial Dilution test is employed. In this test a solution of the anti-bacterial composition is prepared using dimethyl sulphoxide as a solvent. An aliquot of this solution is added to the first of a series of tubes containing trypticase soy broth, thus resulting in a fluid mixture of broth with a certain concentration of anti-bacterial composition. This concentration is thus reduced serially by removing an aliquot from the first tube and adding it to the second tube, and so on, to obtain a series of solutions with decreasing amounts of anti-bacterial composition. The tubes are inoculated with an overnight culture of the test organism and incubated for 48 hours at 37° C. The minimum inhibitory concentration is recorded as the lowest concentration at which no visible growth occurred.

D. Halo Tests

Such tests are generally carried out using culture plates containing in a Petri dish about 20 cc of nutrient agar. There is then added 5cc of seeded agar (prepared by the addition of 2ml of the selected organism grown in an overnight broth culture and then added to 100ml of melted, cool, seed agar). Half-inch discs of special filter paper prepared for biological assay work are dipped in a solution of a selected anti-bacterial composition and laid on the agar in the dish. The assembly is incubated overnight at 35° C and the halos indicating the region of inhibition are measured using a Fisher-Lilly Zone Reader.

If desired, other tests, for example, the so-called "Cade" handwashing test or a direct axillary bacterial count, may be employed as the test procedures.

The following Examples illustrate the invention. In the Examples and elsewhere throughout the specification, all parts, percentages and other proportions are by weight unless otherwise indicated.

EXAMPLE 1

A series of milled and plodded variegated soap bars is prepared in which the soap content is about 94% (balance water), which soap content is derived from a 20% sodium coco soap and an 80% sodium tallow soap. Each of the soaps is prepared containing 1% by weight of 3 - (5 - nitrofurfurylidene) oxindole. Similar bars, "control" bars, are prepared identically except that they do not contain any of the oxindole compound.

Test 1

A modified Cade hand washing test is carried out to determine the anti-bacterial effectiveness as well as the substantivity of the compositions of this invention, as follows:—

1. To determine the average initial bacterial count
 - a. Test subjects are washed with non-antifacterial soap exclusively for two weeks.
 - b. Under supervision, the subjects washed their hands for 60 seconds 5 times.
 - c. The final wash water is collected, samples taken and cultured and the bacteria in the water counted.
2. To determine the anti-bacterial effectiveness in use
 - a. During the 3rd week the subjects used the test soaps exclusively, washing 6 times per day for a total of 30 washings.
 - b. On the third and on the fifth day the bacteria in the wash water is counted and the percent reduction from the initial count is calculated.
3. To determine the substantivity of the test soaps
 - a. During the 4th week the subjects used only a non-antibacterial soap.
 - b. On the fourth and seventh day during the fourth week, bacteria counts are taken to determine the percent reduction from the initial count.

In carrying out the above-described Cade hand washing tests with the soaps of this Example containing 1% active oxindole compound, it was found that on the third and fifth day during the third week the percent reduction from the initial count was better than 99%. It was further found that the residual effectiveness of the soap on the fourth and seventh day during the fourth week was outstanding in comparison to the control and other commercial anti-bacterial soaps.

Test 2

Tests of the minimum inhibitory concentration necessary completely to suppress the growth of the selected organism using the Serial Dilution test described above, indicate that the combination of the oxindole and soap gives values against *A. coli* and *Staph. aureus* of $1:2.4 \times 10^6$ — $1:60 \times 10^6$, and against *C. albicans* a value as high as $1:3 \times 10^6$ is obtained.

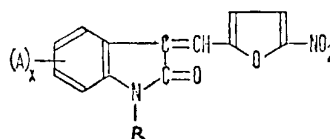
Test 3

In halo tests carried out as described above, the oxindole soap combination gives outstanding zones of inhibition, as evidenced by exceptionally large halos.

EXAMPLE 2

Tests 1, 2 and 3 are each repeated separately employing each of the following oxindole compounds.

- 5 a. 5 - bromo - 3(5 - nitrofurfurylidene) oxindole;
- b. 5 - nitro - 3(5 - nitrofurfurylidene) oxindole;
- 10 c. 5 - acetamido - 3(5 - nitrofurfurylidene) oxindole;
- d. 5 - benzamido - 3(5 - nitrofurfurylidene) oxindole;
- e. 5 - p - chloro - benzamido - 3(5 - nitrofurfurylidene) oxindole;
- 15 f. 6 - acetamido - 3(5 - nitrofurfurylidene) oxindole;
- g. 4 - acetamido - 3(5 - nitrofurfurylidene) oxindole;
- 20 h. 5 - methyl - 3(5 - nitrofurfurylidene) oxindole;
- i. 5 - hydroxy - 3(5 - nitrofurfurylidene) oxindole;
- j. 5 - methoxy - 3(5 - nitrofurfurylidene) oxindole;
- 25 k. 5,7 - dibromo - 3(5 - nitrofurfurylidene) oxindole.



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wherein A represents C_1-C_{30} alkyl, C_1-C_{30} alkoxy, C_2-C_{30} alkoxyalkyl, hydroxy, halogen, carboxy, C_2-C_{30} carbalkoxy, nitro, amino, C_1-C_{30} mono- or di-alkylamino, C_2-C_{30} acylamino, C_1-C_{30} alkylsulphonyl or C_2-C_{30} acyloxy; R represents hydrogen or C_2-C_{30} acyl; and x represents 0 to 4; as the sole or partial colouring agent for the discrete regions.

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2. A composition as claimed in Claim 1 wherein the oxindole compound is 3 - (5 - nitrofurfurylidene) oxindole.

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3. A composition as claimed in Claim 1 or Claim 2 wherein the oxindole compound is present in an amount from 0.01% to 10% by weight of the composition.

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4. A composition as claimed in any of the preceding claims wherein the detergent is a soap.

5. A composition as claimed in Claim 4 wherein the soap is a coconut oil-tallow soap.

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6. A composition as claimed in Claim 5 wherein the soap is an 80% tallow-20% coconut oil soap.

7. A variegated soap bar comprising a matrix of a base colour supplied by the soap and regions of a contrasting colour the regions containing an oxindole compound as defined in Claim 1 or Claim 2, as the sole or partial contrasting colouring agent.

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8. A soap bar as claimed in Claim 7 in which the base colour is white, off-white or ivory and the regions are predominantly red.

9. A soap bar as claimed in Claim 7 or Claim 8 in which the oxindole compound is present in an amount from 0.01% to 10% by weight of the bar.

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10. A soap bar as claimed in any of Claims 7 to 9 of marbled appearance.

EXAMPLE 3

Following the procedure in United States Patent No. 3,485,905, a red and white variegated soap bar is produced containing 1% of the oxindole compound of Example 1 in the same soap as described in that Example. The source of the red colour is the oxindole compound itself, which is a deep red pigment.

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EXAMPLE 4

The general procedure of United States Patent No. 3,519,054 is followed, particularly Example 3, except that all blue pigments and colourings are omitted and the 5 parts (see Example 1) for colouring are coloured with one part of the oxindole of Example 1. A white matrix detergent containing about 5 parts red particles (about 90% within the range of -8+60 U.S. Sieve No.) is obtained. The detergent contains about 1% oxindole anti-bacterial agent.

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WHAT WE CLAIM IS:—

1. A multi-coloured detergent composition comprising a detergent and, in discrete regions of the composition which contrasts in colour to other regions of the composition, an anti-

KILBURN & STRODE,
Chartered Patent Agents,
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Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa, 1975.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.